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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/063,569 | 05/02/2002 | Dan L. Eaton | P3230R1C49 | 9761 |

30313 7590 01/07/2005

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| EXAMINER | |
|---|---|
| HUNNICUTT, RACHEL KAPUST | |
| **ART UNIT** | **PAPER NUMBER** |
| 1647 | |

DATE MAILED: 01/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/063,569 | EATON ET AL. | |
| | Examiner | Art Unit | |
| | Rachel K. Hunnicutt | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-13 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-13 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 02 May 2002 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Specification*

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see, for example, p. 31 and 35). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The use of the trademarks SEPHADEX™ (p. 86), SEPHAROSE™ (p. 86), TWEEN™ (p. 96), PLURONICS™ (p. 96), MATCHMAKER™ (p. 97), LUPRON DEPOT™ (p. 111), LIFESEQ™ (p. 113), SUPERSCRIPT™ (p. 114), KLENTAQ™ (p. 117), QIAQUICK™ (p. 119), POROS™ (p. 126), SUPERFECT™ (p. 129), FUGENE™ (p. 129), and BACULOGOLD™ (p. 131) have been noted in this application. They should be capitalized (in all capital letters) wherever they appear and be accompanied by the generic terminology. Applicants should check the rest of the specification for other trademarks and for other references to the above-cited trademarks.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-13 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Claims 1-13 are directed to polypeptides comprising SEQ ID NO: 64. The claimed polypeptides are not supported by either a specific and substantial asserted utility or a well-established utility.

A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" use for the claimed invention. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966):

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

Uses such as assaying for binding partners (p. 95), using polypeptides as molecular weight markers (p. 92), and screening for agonists and antagonists of PRO3566 (p. 95-99) are useful only in research to determine the function of the encoded protein itself. There is no "specific benefit in currently available form" to be derived from such studies. Applicants also teach that the PRO3566 polypeptide or agonists or antagonists of PRO3566 may be used in the preparation of medicaments or in gene therapy (Examples 12 and 13). Even though Applicants teach that PRO3566 DNA is "more highly expressed" in normal skin cells and esophageal tumor cells when compared to melanoma tumor cells and normal esophageal cells, respectively (p. 142), there is no guidance in the specification as to how high levels are. The asserted utility in diagnosis and treatment of the aforementioned cancers is not substantial. It is not clear whether the overexpression of PRO3566 is statistically significant and whether such overexpression is correlated to the overexpression of the claimed protein or whether it is due to aneuploidy. The specification fails to disclose the biological significance of this overexpression. The specification also does not teach whether the overexpression is the cause or the result of the tumors. The only thing Applicants teach is that the gene was "more highly expressed", and this does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any diseases. Clearly further research and experimentation would be required to find out whether PRO3566 is useful as asserted. See *Brenner v. Manson*, noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Further research would be required to determine how and if PRO3566 is involved in any disease.

A substantial utility, *by definition*, is a utility that defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real

world" context of use is not a substantial utility. In the instant case, the overexpression of the PRO3566 in normal skin cells and esophageal tumor cells (if significant), at the most, is an interesting invitation for further research, experimentation and confirmation as to whether the PRO3566 is useful as a diagnosis marker, or suitable as a therapeutic target for treatment of the tumors. Therefore, the claimed invention is not considered substantial.

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The specification fails to assert any activity for the claimed polypeptide. Applicants have not asserted that PRO3566 is a member of any protein family nor have Applicants asserted that PRO3566 is homologous to any known proteins. Thus, PRO3566 lacks a well-established utility.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 10, and 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation that the encoded protein comprises an "extracellular domain...lacking its associated signal peptide" (claim 1, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of maturation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well

established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1-5 and 12-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, were it enabling for an isolated polypeptide comprising SEQ ID NO: 64 or least the mature form of SEQ ID NO: 64, would still not reasonably provide enablement for polypeptides having at least 80%, 85%, 90%, 95% or 99% amino acid sequence identity to the polypeptide of SEQ ID NO: 64. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a polypeptide having at least 80%, 85%, 90%, 95% or 99% amino acid sequence identity to the polypeptide of SEQ ID NO: 64, referred to as PRO3566. There are no functional limitations in the claims. Applicants have taught the polypeptide of SEQ ID NO: 64, as well as the putative signal sequence. However, there is no function known in the art to be associated with such a polypeptide, nor have Applicants provided any evidence of functions for the polypeptide.

The claims encompass an unreasonable number of inoperative polypeptides, which the skilled artisan would not know how to use. The specification provides no teachings as to the structural or related functional characteristics of this protein. There are no working examples of polypeptides less than 100% identical to the polypeptide comprising SEQ ID NO: 64. The skilled artisan would not know how to use non-identical polypeptides on the basis of teachings in the prior art or specification. The claims are broad because they do not require the claimed polypeptide to be identical to the disclosed sequence, polypeptides that are at least 80%, 85%,

90%, 95%, or 99% identical to SEQ ID NO: 64 could have structures and functions vastly different from that of SEQ ID NO: 64, and because the claims have no functional limitation.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of transmembrane proteins, and lack of knowledge about function(s) of encompassed polypeptides structurally related to SEQ ID NO: 64, the lack of direction or guidance for using polypeptides that are not identical to at least the mature form of SEQ ID NO: 64, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claims 1-5 and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the encoded polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the protein has the disclosed activity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in

possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 64 but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Oka *et al.* (NCBI Accession No. BAA88132, December 8, 1999). Claims 1-5 are drawn to polypeptides having at

least 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 64. Oka et al teach a sequence which is 99% identical to SEQ ID NO: 64. Thus, claims 1-5 are anticipated by Oka *et al.*

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Janer *et al.* (NCBI Accession No. AC006163, December 8, 1998). Claims 1-4 are drawn to polypeptides having at least 80%, 85%, 90%, or 95% sequence identity to SEQ ID NO: 64. Janer *et al.* teach a nucleic acid sequence which encodes a polypeptide 98% identical to SEQ ID NO: 64 (see attached alignment). Thus, claims 1-4 are anticipated by Janer *et al.*

***Conclusion***

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH
1/6/05

JANET ANDRES
PRIMARY EXAMINER